

### **REMARKS/ARGUMENTS**

Claims 1, 5, 7-8, 13, 17-22, 24-31 and 33-37 are pending in the captioned application. Claims 30, 36 and 37 have been withdrawn. Claims 1, 5, 7-8, 13, 17-22, 24-29, 31 and 33-35 are under examination and stand rejected. Applicants respectfully request reconsideration and allowance of the claims in view of the amendments and the following arguments.

Claims 22, 24, 31 and 33-35 stand rejected under 35 U.S.C. §112, first paragraph, for not providing an adequate written description. Applicants respectfully disagree. However, in an effort to expedite the prosecution, Applicants have cancelled these claims rendering the rejection moot.

Claims 1, 5, 7-8, 13, 17-21, 25-29, 31 and 33-35 stand rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of Cooper et al. (Anal. Biochem. 277:196, 2000), Niemeyer et al. (Anal. Biochem. 268:54, 1999), and Nikiforov et al. (US 5,610,287). Applicants respectively disagree.

Applicants first submit that the currently claimed invention relates to immobilization of targets to surfaces where the target and surface both have a negative charge. In particular, it relates to targets with high negative charge which are immobilized to surfaces with high negative charge. This is realized by using cationic detergents in vesicle format to provide a carrier for the target such as oligonucleotides which shields the charge of DNA and lowers the repulsion from a highly negatively charged surface. To clarify the claimed invention, Applicants have amended claim 1,

including the limitations of now cancelled claims 5, 7, 18-20. Further support for the claim amendment can be found in the specification, see paragraph 73 of the published US patent application.

The Examiner suggested exchanging the salts in Cooper and Niemeyer for detergents in Nikiforov. Applicants submit that this is not relevant for the claimed invention because it does not work for this combination of ligand and surface properties. In Nikiforov, the vesicle is fused to a hydrophobic surface. Therefore, Nikiforov's hydrophobic anchoring would not work on highly charged surfaces. Nikiforov does not describe shielding of the charge of an oligonucleotide. The purpose of the detergent in Nikiforov is to achieve hydrophobic interaction which enables the immobilization. In contrast, the immobilization into carboxymethyl-modified dextran polymer hydrogel matrix is greatly facilitated when a target molecule can be trapped by electrostatic forces as in the currently claimed invention. By using salt, these forces are shielded as charges on both target and surface are masked. This leads to prevention of electrostatic interactions and thereby prevents efficient immobilization at practical target concentrations.

Thus, Applicants submit that it is not possible to combine the immobilization via binding pairs (Cooper and Niemeyer) and immobilization via detergent (Nikiforov) and arrive at the presently claimed invention. In Nikiforov, initially there is association in solution between the negatively charged oligonucleotides and the positively charged detergent-like molecules. The number of detergent molecules that associate with each oligonucleotide molecule will depend on the oligonucleotide

length, but should be significantly higher than one in the case of a 25-mer oligonucleotide. This association of oligonucleotides with detergents containing a hydrophobic tail will render the oligonucleotide significantly hydrophobic and will lead to its immobilization to the plate surface by hydrophobic interactions. In effect these molecules appear to act as a linker between the hydrophobic areas of the plate and the charged phosphate backbone of the oligonucleotide (e.g., the oligonucleotide is not shielded).

If the concentration of the detergent molecules in Nikiforov would be higher than their cmc, micelles will form. Although oligonucleotides might still interact with the detergent molecules, they will be included in the micelles, and since the micelles have a hydrophobic core that is completely surrounded by a polar surface, no hydrophobic interactions with the surface will occur and therefore oligonucleotide immobilization will be diminished or prevented. Applicants submit that as such, Nikiforov actually teaches away from the presently claimed invention.

Applicants respectfully assert that the claims are in allowable form and earnestly solicit the allowance of the claims 1, 8, 13, 17, 21 and 25-29.

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Early and favorable consideration is respectfully requested.

Respectfully submitted,

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